

AMENDMENTS TO THE CLAIMS

1.-25. (Canceled)

26. (Currently amended) A method for ~~determining, in~~ aiding in the determination of whether a mammal, ~~the susceptibility is susceptible to or at risk of a disease associated with β -amyloid formation and/or aggregation, for determining, in a mammal, the risk of developing a disease associated with β -amyloid formation and/or aggregation, for screening of the clearance of β -amyloid deposits in a mammal, and/or for predicting the level of β -amyloid burden in a mammal,~~ said method comprising:

- (a) determining, in a first sample obtained from said mammal, the total amount of N-terminal truncated and/or post-translationally modified β -amyloid variant;
- (b) comparing the amount of β -amyloid variant determined in step (a) with the amount of said N-terminal truncated and/or post-translationally modified β -amyloid variant typically present in control samples obtained from one or more patients known to suffer, or known not to suffer, from a particular disease associated with β -amyloid formation and/or aggregation;
- (c) concluding, from the comparison in step (b), whether the mammal is susceptible to or at risk of a disease associated with β -amyloid formation and/or aggregation, ~~or whether the mammal is at risk of developing a disease associated with β -amyloid formation and/or aggregation, whether the β -amyloid deposition in the mammal is cleared, or what the level of β -amyloid burden is in said mammal.~~

27. (Cancelled)

28. (Cancelled)

29. (Currently amended) The method of claim 26 comprising:

- (a) determining in the first sample, the amount of one or more N-terminal truncated and/or post-translationally modified β -amyloid variant(s);
- (b) comparing the amount determined in step (a) with the amount of the particular N-terminal truncated and/or post-translationally modified β -amyloid variant(s) typically present in control samples obtained from one or more patients known to suffer, or known not to suffer, from a particular disease associated with β -amyloid formation and/or aggregation in the second sample;

- (c) concluding, from the comparison of step (b), whether the mammal is susceptible to or at risk of a disease associated with β -amyloid formation and/or aggregation, ~~whether the mammal is at risk of developing a disease associated with β -amyloid formation and/or aggregation, whether the β -amyloid deposition in the mammal is cleared, and/or what the level of β -amyloid burden is in the mammal.~~

30. (Currently Amended) The method of claim 29 for aiding in the determination of whether a mammal is susceptible to or at risk of a disease associated with β -amyloid formation and/or aggregation by measuring ~~predicting the~~ said mammal's level of β -amyloid burden in a mammal, the method further comprising:

- (a) administering to said mammal a composition for eliciting an immune response or a ~~therapeutic composition comprising an~~ one or more particular N-terminal truncated and/or post-translational modified [[A]] β -amyloid variants ~~peptide~~;
- (b) determining in a biological fluid sample obtained from said mammal the total amount of N-terminal truncated and/or post-translationally modified β -amyloid variant;
- (c) subtracting from the total amount of said β -amyloid variant determined in step (b) the amount of the administered β -amyloid variant(s) present in said biological fluid sample.
- (d) comparing the amount of β -amyloid variant determined in step (c) with the amount of said the non-administered ~~N-terminal truncated and/or post translationally modified β -amyloid variant~~ typically present in control samples obtained from one or more patients known to suffer, or known not to suffer, from a particular disease associated with β -amyloid formation and/or aggregation;
- (~~d~~e) concluding, from the comparison in step ([c]d) ~~what~~ the level of β -amyloid burden is in said mammal.

31. (Withdrawn) The method of claim 26 wherein said N-terminal truncated β -amyloid variant starts at position 2, 3, 4, 5, 6, 7, 8, 9, or 10 of β -amyloid.

32. (Withdrawn) The method of claim 31 wherein said N-terminal truncated β -amyloid variant starts at position 2, 3, 4, 5, 8, 9, or 10 of β -amyloid.
33. (Withdrawn) The method of claim 32 wherein said N-terminal truncated β -amyloid variant starts at position 3, 4, 5, 8, or 9 of β -amyloid.
34. (Withdrawn) The method of claim 31 wherein said β -amyloid variant is selected from the group consisting of $A\beta(2-42)$, $A\beta(3-42)$, $A\beta(4-42)$, $A\beta(5-42)$, $A\beta(6-42)$, $A\beta(7-42)$, $A\beta(8-42)$, $A\beta(9-42)$ and $A\beta(10-42)$.
35. (Withdrawn) The method of claim 26 wherein the post-translationally modified β -amyloid variant is modified by methylation or pyroglutamylation.
36. (Withdrawn) The method of claim 35 wherein the methylation is present at position 1, 2, 4, or 6 of an N-terminal truncated β -amyloid variant.
37. (Withdrawn) The method according to claim 35 further characterized in that the pyroglutamylation is present at position 3 of an N-terminal truncated β -amyloid variant starting at position 3 of β -amyloid.
38. (Cancelled)
39. (Currently amended) The method of claim ~~29-26 for determining in a mammal, the susceptibility to a disease associated with β -amyloid formation and/or aggregation, or for determining, in a mammal, the risk of developing a disease associated with β -amyloid formation and/or aggregation~~ comprising:
- (a) determining, in a sample obtained from said mammal~~[[:]]~~ the amount of antibody or reactive T-cells specific for an N-terminal truncated and/or post-translationally modified ~~[[A]] β -amyloid variant-peptide~~;
 - (b) comparing the amount determined in step (a) with the amount of the antibody or reactive T-cells~~in a control mammal~~ typically present in control samples obtained from one or more patients known to suffer, or known not to suffer, from a particular disease associated with β -amyloid formation and/or aggregation;

(c) concluding, from the comparison in step (b), whether the mammal is susceptible to or at risk for a disease associated with β -amyloid formation and/or aggregation ~~or whether the mammal is at risk of developing a disease associated with β -amyloid formation and/or aggregation;~~

wherein an increased amount of antibody or reactive T-cells specific for ~~[[i)]N-terminal truncated and/or post-translationally modified [[A]] β -amyloid variant peptide~~ is an indication that the mammal is susceptible to, or at risk of, developing a disease associated with $A\beta$ formation and/or aggregation.

40. (Previously presented) The method of claim 26 wherein at least one of the first and second samples is a brain extract sample or a body fluid sample.

41. (Currently Amended) The method of claim 40 wherein the body fluid sample is a blood sample or a cerebrospinal fluid (CSF) sample.

42. (Previously presented) The method of claim 26 wherein the disease associated with β -amyloid formation and/or aggregation is Alzheimer's disease (AD).

43. (Withdrawn) The method of claim 26 wherein the susceptibility to Alzheimer's disease (AD) or the risk of developing AD is determined by detecting $A\beta(5-42)$ or $A\beta(8-42)$ in a body fluid sample obtained from the mammal.

44.-54. (Cancelled)

55. (New) The method of claim 29 for aiding in the determination of whether a mammal is susceptible to or at risk of a disease associated with β -amyloid formation and/or aggregation by measuring the clearance of β -amyloid deposits in said mammal, the method further comprising:

(a) administering to said mammal a composition for eliciting an immune response or comprising one or more particular N-terminal truncated and/or post-translational modified β -amyloid variants;

- (b) determining in a biological fluid sample obtained from said mammal the total amount of N-terminal truncated and/or post-translationally modified β -amyloid variant;
 - (c) subtracting from the total amount of said β -amyloid variant determined in step (b) the amount of the administered β -amyloid variant(s) present in said biological fluid sample.
 - (d) comparing the amount of β -amyloid variant determined in step (c) with the amount of the non-administered variants typically present in control samples obtained from one or more patients known to suffer from a particular disease associated with β -amyloid formation and/or aggregation;
 - (e) concluding, from the comparison in step (d) the amount of β -amyloid cleared.
56. (New) The method of claim 29 wherein said N-terminal truncated β -amyloid variant starts at position 4 of β -amyloid.
57. (New) The method of claim 56 wherein said β -amyloid variant is $A\beta(4-42)$.
58. (New) The method of claim 29 wherein the post-translationally modified β -amyloid variant is modified by methylation.
59. (New) The method of claim 58 wherein the methylation is present at position 4 of an N-terminal truncated β -amyloid variant.
60. (New) The method of claim 29 wherein the susceptibility to Alzheimer's disease (AD) or the risk of developing AD is determined by detecting $A\beta(5-42)$ in a body fluid sample obtained from the mammal.
61. (New) The method of claim 26 wherein the amount of N-terminal truncated and/or post-translationally modified β -amyloid variant is determined by 2-D electrophoresis or mass spectrometry or both.
62. (New) The method of claim 26 wherein the total amount of β -amyloid is detected using an antibody that binds to a β -amyloid epitope towards the C-terminus.

63. (New) The method of claim 29 wherein the amount of one or more N-terminal truncated and/or post-translationally modified β -amyloid variants is detected using an antibody that binds an epitope at the N-terminus of said variants.